This question paper contains 5 printed pages.

6858 *Your Roll No*

M.Sc. – Ph.D. / IV Sem. **J**

BIO-MEDICAL SCIENCES

Bio–1003 Human Genetics

Time : 3 hours *Maximum Marks* : 75

(Write your Roll No on the top immediately on receipt of this question paper)

Use separate answer-books for Section A and Section B.

Attempt six questions in all Question Nos. 1 and 5 are compulsory Out of the four questions answer at least one question from each Section

Section A

Q1. Answer the following briefly **10 marks**

(a) Between microsatellite markers and SNPs, which are more informative markers, why?

(b) It is often said, that complex diseases follow non-Mendelian inheritance Does it mean the Mendel's laws of segregation do not apply for complex diseases? Explain

(c) What is Alu-PCR? Where is it useful?

(d) Mention three co-dominant markers in the human genome Why do they show co-dominance.

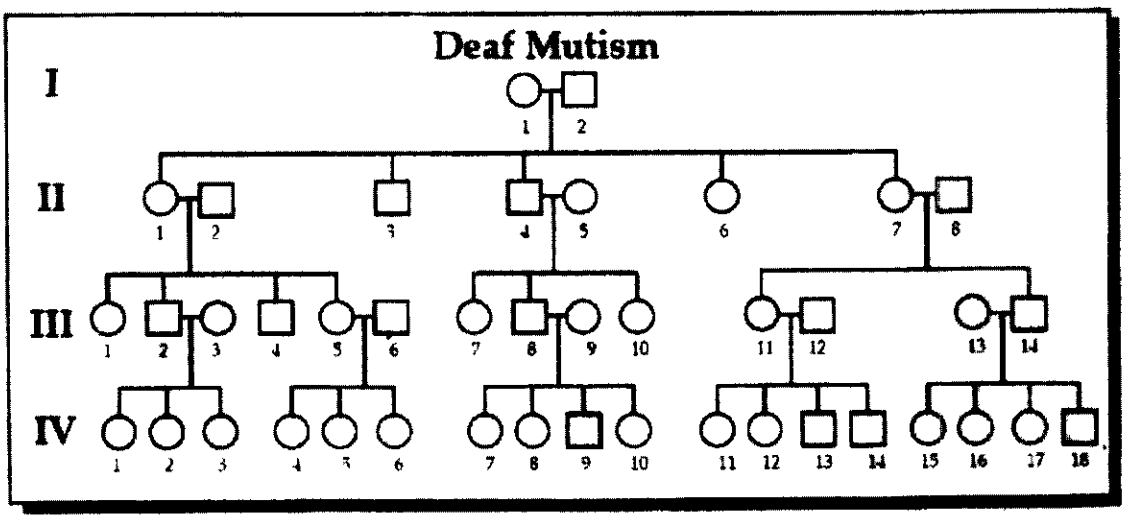
(e) The female to male ratio of genetic length of chromosome 22, is 1.5 according to Marshfield map What does this mean?

Q2. A. (i) In the pedigree shown below, how can parents 1 and 2 of generation I have a deaf child though they are unaffected? 2 marks

(ii) Why is the disease not seen in parents of 8 and 11 of III generation? Explain 2 marks

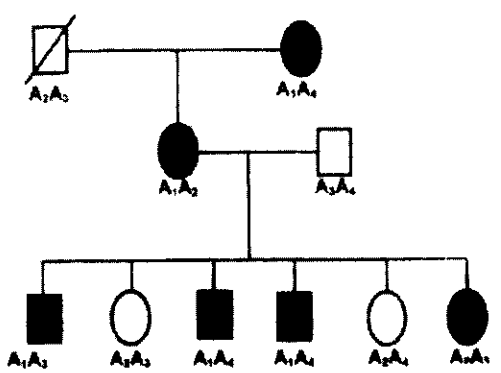
(iii) In this pedigree who are the individuals whose genotype you cannot deduce? Why? 2 marks

P T O.



B. What are somatic cell hybrid and radiation hybrid (RH) cells? How can they help in mapping non-polymorphic markers like STS and EST? 4 marks.

C. Calculate the LOD score for possible linkage between a disease causing gene and a polymorphic marker A in the pedigree given below at θ values of 0.1 and 0.2. The filled symbols denote affected individuals 5 marks



Q3. A. In linkage analysis, when parental genotypes are not available it is important to know the allele frequency in the population to which the parents belong. Is this true? Justify. **3 marks**

B. Why is penetrance of a mutation considered important in genetic mapping? **3 marks.**

C. Enumerate four important consequences of copy number variation on genome function and human biology **3 marks**

D. How can you enhance the resolution of CGH method to detect genetic variation between test and reference genomes? **2 marks.**

E. Explain how pharmacogenomics can be applied to prevent and minimise adverse drug reactions with an example? **5 marks**

Q4 The table above lists diseases that are dominantly inherited and show incomplete penetrance.

(a) Based on the function of the genes given explain the basis of dominant inheritance and incomplete penetrance in disease 1,2, 5 and 6 **6 marks**

(b) Draw a hypothetical pedigree for any one disease to show dominant inheritance and incomplete penetrance **4 marks**

(c) As per the given data, do you agree that Brachydactyly appears as a oligogenic disease Justify. **3 marks**

(d) Do you think homozygous Brachydactyly Type D father and Type B1 mother can have a normal child if locus heterogeneity is true in this case. Justify your response **2 marks.**

Number	Disease	Gene	Chromosome	Function
1	Brachdactyly, Type D	HOXD13	2q31-q32	Transcription factor
2	Brachdactyly, Type B1	ROR	9q22	Receptor Tyrosine kinase
3	Breast Cancer 2. Early onset	BRCA2	13q12 3	Transcription factor
4	Breast cancer 1 Ovarian cancer	BRCA1	17q21	Transcription Factor
5	Brugada Syndrome	SCN5A	3p21	Sodium Channnel, voltage -gated
6	Caffey Disease	COL1A1	17q21 31-q22	Collagen

Section B

Q5. Answer the following briefly (Compulsory)

(a) Multipoint analysis is better than single point analysis in genetic mapping studies Comment. **1.5 marks**

(b) What are the advantages of using F- factor based vectors for cloning **1.5 marks**

(c) What is the advantage of representing differential expression as log transformed values in microarray experiments. **2 marks**

Q6. Answer the following questions.

(a) What are the four HAPMAP populations? **(2)**

(b) In the Indian Genome Variation consortium how many populations were included in the study? **(1)**

(c) Amongst the three factors, geography, ethnicity and language, name the most and least important contributors towards the population diversity of India. **(2)**
(d) You expect more diversity between any two urban caste populations or between two isolated tribal populations, why? **(2)**
(e) What is Hardy-Weinberg equilibrium? Write the assumptions that are associated with it. **(1+2)**
(f) What is population stratification? Between a project on genetics of Cystic Fibrosis and another on genetics of Schizophrenia, which will be more affected by population stratification? Why? **(2+1+2).**

Q7.A. What is linkage disequilibrium (LD)? Why it is important to know the LD patterns of different populations? What are tagged SNPs? Between African and European population, for any given region of the genome, which will have more number of tag SNPs and Why? **(1+2+1+1+2)**

B. Linkage mapping studies are not successful in identifying genes involved in complex disorders Discuss **3 marks**

C. Explain why the availability of physical and genetic maps was a prerequisite in the publicly funded Human Genome Project **3 marks.**

D. How accurate overlaps in the clones are detected in the Whole Genome Shotgun Sequencing approach. **2 marks**

Q8. Study the following figures and figure legends and provide answers to the questions that follow each figure

8A

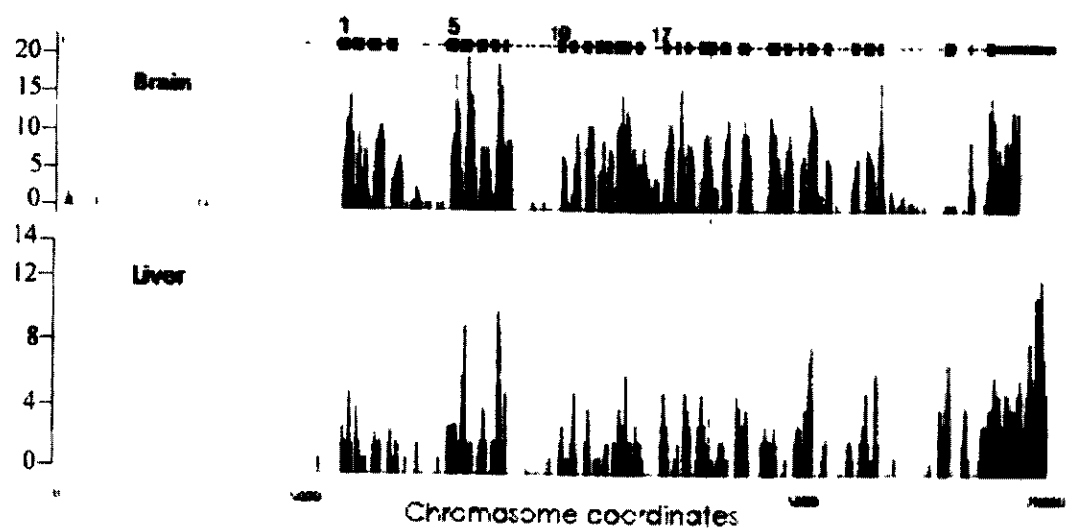


Fig.1. The gene structure (exons in rectangles, introns as thin line) of YFG1 gene is shown in the top panel. Mouse poly(A) selected RNAs were subjected to RNA-seq analysis. The normalized reads(Y-axis) from brain and liver after aligning to the YGF1 gene are displayed in the graphs below the gene structure.

Fill in the blanks/ answer the questions: (1+1+1+1+3+3)

1 The gene is expressed at a relatively higher level in the_____, as compared to _____

2 The gene has atleast _____ polyadenylation sites

3. Counting the first exon as one marked with '1' at the top, _____exon is a liver specific exon.

4. The 3' splice site of the ____ exon is frequently skipped in the brain.

5. If the experiment was done on total RNA instead of polyadenylated RNA, would the profile be different? How?

6 An antibiotic discovered recently can act as a pharmacological inhibitor of splicing. The experiment is done after acute treatment with this agent, how would the profile be different?

8B. Figure2

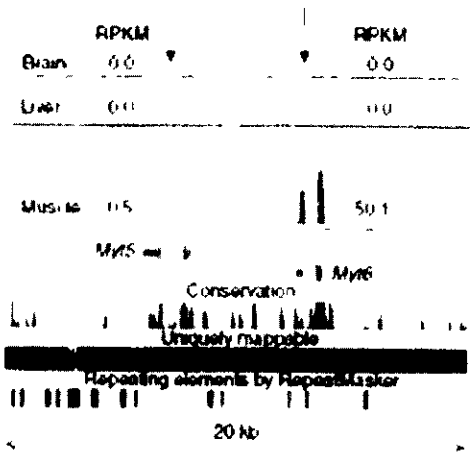


Fig.2. Mouse poly(A)-selected RNAs were subjected to RNA-seq analysis The reads(arrow) from brain, liver and skeletal muscle for a 20-Kb region of chromosome 10 containing two paralogous genes Myf5 and Myf6 are presented. Genome organization of the 20kb region is displayed below.The RPKM values for the same are presented as a table in the top panel

Based on this, Myf6 is specifically expressed in the _____ tissue. 1 mark.

Is Myf5 likely to be a pseudogene?Justify your answer 4 marks